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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/754,083	01/05/2001	Edward Green	00487.00007	4709

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EXAMINER
RAO, MANJUNATH N

ART UNIT	PAPER NUMBER
1652	

DATE MAILED: 09/18/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	09/754,083	GREEN ET AL.	
	Examiner	Art Unit	
	Manjunath N Rao	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 July 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *15-25* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *05 January 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *9* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-25 are presently pending in this application.

Election/Restrictions

Applicant's election of Group I, claims 1-14 in Paper No. 11 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Priority

Acknowledgment is made of applicant's claim for foreign priority under 35 U.S.C. 119(a)-(d). Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

Drawings submitted in this application are accepted by the Examiner for examination purposes only.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1 and claims 2-13 which depend from claim 1 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase "but has

solely native alcohol dehydrogenase function". While the meaning of the term "solely" is clear to the Examiner, the use of the above term by the applicants in the context of the above claim is not clear to the Examiner. This is because it is not clear to the Examiner as to whether applicants are using the term with respect to the "bacterium that is being transformed" or with respect to the "pyruvate decarboxylase or a functional equivalent thereof" which has alcohol dehydrogenase activity. Even if the term is considered to be related to the bacterium, it is still not clear because, the claim as written would then indicate that the bacterium produces only alcohol dehydrogenase enzyme and nothing else. Simply deleting the term "solely" would render the claim clear.

Claim 1 and claims 2-13 which depend from claim 1 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 1 recites the phrase"or a functional equivalent thereof". While applicants claim that the heterologous gene encodes pyruvate decarboxylase, the use of the above phrase in addition, renders the claim indefinite because of the scope of the above phrase is not clear to the Examiner.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-14 are directed to Gram positive bacterium transformed with a heterologous gene encoding pyruvate decarboxylase or a functional equivalent thereof. Claims 1-14 are rejected under this section of 35 USC 112 because the claims are directed to a genus of polypeptides including modified polypeptide sequences, modified by at least one of deletion, addition, insertion and substitution of an amino acid residue that have not been disclosed in the specification. No description has been provided of the modified polypeptide sequences encompassed by the claim. No information, beyond the characterization of the function has been provided by applicants which would indicate that they had possession of the claimed genus of modified polypeptides. The specification does not contain any disclosure of the structure of all the polypeptide sequences, including fragments and variants within the scope of the claimed genus. The genus of polypeptides claimed is a large variable genus including peptides which can have a wide variety of structures. Therefore many structurally unrelated polypeptides are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that applicant had possession of the claimed invention at the time the instant application was filed.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 12-14 are rejected because the invention appears to employ novel vectors and novel strains of microorganisms. Since the vectors and microorganisms are essential to the

claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The claimed plasmids' sequences or the microorganisms are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. The enablement requirements of 35 U.S.C. § 112 may be satisfied by a deposit of the plasmids/microorganisms. The specification does not disclose a repeatable process to obtain the vectors/microorganisms and it is not apparent if the DNA sequences are readily available to the public. Accordingly, it is deemed that a deposit of the plasmid and microorganisms should have been made in accordance with 37 CFR 1.801-1.809.

It is noted that applicants have deposited the plasmid and the microorganisms but there is no indication in the specification as to public availability. As the deposit has been made under the terms of the Budapest Treaty, an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 2, 8, 11 are rejected under 35 U.S.C. 102(b) as being anticipated by Danilevich et al. (Molecular Biology, 1994, Vol. 28(1):158-166). This rejection is based upon the public availability of a printed publication in this country in which the invention was described more than one year prior to the date of the application for patent. Claims 1, 2, 8, 11 of the instant application are drawn to a Gram positive bacterium which has been transformed with a heterologous gene encoding pyruvate decarboxylase or a functional equivalent thereof, but has native alcohol dehydrogenase activity, wherein the bacterium is a *Bacillus sp.*, wherein the heterologous gene is from *Z.mobilis* and wherein the Gram positive bacterium has been transformed with a plasmid comprise the heterologous gene. Danilevich et al. disclose an identical gram positive bacterium belonging to the *Bacillus sp.* which has been transformed with a plasmid comprising the heterologous gene from *Z.mobilis* encoding pyruvate decarboxylase. Thus Danilevich et al. anticipate claims 1, 2, 8, 11 of this application as written.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-8, 10-11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Danilevich et al. as applied to claims 1, 2, 8, 11 above, and further in view of Hartley et al. (Biotechnol., 1983, Vol. :895-905), Morris et al. (Biochem. Biophys. Res. Commun. May.29, 1987, Vol. 145(1):390-396.) and the common knowledge in the art of molecular biology.

Claims 1-8, 10-11 in this instant application are drawn to a Gram positive bacterium which has been transformed with a heterologous gene encoding pyruvate decarboxylase or a functional equivalent thereof, but has native alcohol dehydrogenase activity, wherein the bacterium is a *Bacillus sp.*, selected from a group among which one is *B.stearothermophilus*, wherein the gene encoding lactate dehydrogenase has been inactivated by homologous recombination, wherein the heterologous gene is from *Z.mobilis* or *S.cerevisiae* and wherein the heterologous gene is incorporated into the chromosome of the bacterium or the Gram positive bacterium has been transformed with a plasmid comprising the heterologous gene.

The reference of Danilevich as it applies to claims 1, 2, 8 and 11 has been argued above. As can be seen the reference does not teach the use of a thermophilic strain such as *B.stearothermophilus* in place of *B.circulans* and also the reference does teach that the lactate dehydrogenase be inactivated or that the heterologous gene be operatively linked to the LDH promoter from a bacillus strain.

Hartley et al. teach the advantages of using a thermophilic microorganism such as *B.stearothermophilus* for production of ethanol. The reference teaches a "metabolic steering" strategy of developing strains of *B.stearothermophilus* for production of ethanol. The reference teaches that knocking out (i.e., inactivating) lactate dehydrogenase would steer the metabolic pathway of the above microorganism for production of more ethanol, as this is the enzyme that steers the aerobic pathway towards production of lactic acid rather than acetate and ethanol. The reference also teaches that alternatively, one of skilled in the art could try a recombinant approach by introduction of a gene for pyruvate decarboxylase from yeast or *Zymomonas*. The

reference provides methods to select mutants that are lactate non-producers or low lactate producers in which the lactate dehydrogenase is inactivated.

Therefore, with the reference of Danilevich et al. which teaches the introduction of *Z.mobilis* pyruvate decarboxylase into *B.subtilis* and the reference of Hartley et al. which teaches the advantages of using a thermophilic *Bacillus* which has been genetically modified for alcohol production, it would have been obvious to one of ordinary skill in the art to transform *B.stearothermophilus* instead of *B.subtilis* as taught by Danilevich et al. and develop a strain for production of ethanol. With the common knowledge prevailing in the art of molecular biology, it would have been obvious to use methods in which the heterologous gene is introduced through a plasmid or incorporate it into the chromosome of the host bacterium. One of ordinary skill in the art would have been motivated to do so as Hartley et al. teach that use of thermophilic bacteria for production of ethanol has certain economic advantages over other fermentation methods. One of ordinary skill in the art would have a reasonable expectation of success since Danilevich et al. demonstrate the transformation of a *Bacillus sp.* with the pyruvate decarboxylase of *Z.mobilis* and the reference of Hartley et al. suggest the same and in addition provide methods to obtain lactate dehydrogenase non-producers.

Therefore the claimed invention would have been *prima facie* obvious to one of ordinary skill in the art.

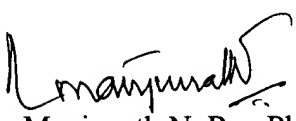
This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any

evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Conclusion

None of the claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Manjunath Rao whose telephone number is (703) 306-5681. The Examiner can normally be reached on M-F from 7:30 a.m. to 4:00 p.m. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, P.Achutamurthy, can be reached on (703) 308-3804. The fax number for Official Papers to Technology Center 1600 is (703) 305-3014. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



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9/17/02